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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

		Application Number	10/048,033
		Filing Date	November 27, 2002
		First Named Inventor	H. Michael SHEPARD
		Art Unit	1615
		Examiner Name	Not Yet Assigned
Total Number of Pages in This Submission	25	Attorney Docket Number	NB 2006.01

ENCLOSURES (check all that apply)

<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance Communication to Group
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Amendment / Reply	<input type="checkbox"/> Petition	<input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> After Final	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address	<input type="checkbox"/> Status Letter
<input type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Terminal Disclaimer	<input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):
<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Request for Refund	Form PTO/SB/08a (5 pages), Form PTO/SB/08b (15 pages), 249 references, postcard receipt
<input checked="" type="checkbox"/> Information Disclosure Statement	<input type="checkbox"/> CD, Number of CD(s) _____	
<input type="checkbox"/> Certified Copy of Priority Document(s)		
<input type="checkbox"/> Response to Missing Parts/ Incomplete Application		
<input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53		

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Antoinette F. Konski Bingham McCutchen LLP
Signature	
Date	January 11, 2005

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Typed or printed name	Mark R. Zimmerman	Date	January 11, 2005
Signature			

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Dated: January 11, 2005

Mary R. Zimmerman

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application for:

H. Michael SHEPARD

Serial No.: 10/048,033

Examiner: Not Yet Assigned

Filing Date: November 27, 2002

Group Art Unit: 1615

For: METHODS FOR TREATING
THERAPY-RESISTANT TUMORS

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

In accordance with 37 CFR §§ 1.97 and 1.98, the items identified on the attached forms PTO/SB/08a and PTO/SB/08b are being brought to the attention of the Examiner for consideration in connection with the examination of the above-identified patent application. The Examiner is requested to make these documents of record. Copies of the documents are being attached hereto. The Examiner is requested to make these documents of record.

I. Timing of the Information Disclosure Statement:

This Information Disclosure Statement is filed:

- With the new patent application submitted herewith (37 C.F.R. § 1.97(a)).
- Within three months after the filing date of the application or within three months after the date of entry of the national stage of a PCT application as set forth in 37 C.F.R. § 1.491.
- Before the mailing date of a first Office action on the merits. In the event, however, that an Office Action has crossed in the mail with this Information

Disclosure Statement, the Commissioner is hereby authorized to charge Deposit Account No. 50-2518 for any fees required pursuant to 37 C.F.R. §§ 1.17(p) or 1.17(i)(1).

This Information Disclosure Statement is filed:

- After the first Office Action and more than three months after the application's filing date; or PCT national stage date of entry filing but, as far as is known to the undersigned, prior to the mailing date of either a final rejection or a notice of allowance, whichever occurs first, and the Commissioner is hereby authorized to charge Deposit Account No.[50-2518] for the fee (\$180) set forth in 37 C.F.R. § 1.17(p) and any additional required fees.

This Information Disclosure Statement is filed:

- After the mailing date of either a final rejection or a notice of allowance, whichever occurred first, and is accompanied by the fee (\$180.00) set forth in 37 C.F.R. § 1.17(i)(1) and a certification as specified in 37 C.F.R. § 1.97(e), as checked below. This document is to be considered as a petition requesting consideration of the Information Disclosure Statement.

The undersigned certifies that:

- Each item of information contained in the Information Disclosure Statement was first cited in any communication mailed from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this information disclosure statement.
- No item of information contained in this information disclosure statement was cited in a communication mailed from a foreign patent office in a counterpart foreign application or, to the knowledge of the undersigned after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

II. Copies of the Cited Items:

- Copies of all of the items listed on the attached forms PTO/SB/08a and PTO/SB/08b are enclosed.
- Copies of only the following items listed on the attached forms PTO/SB/08a and PTO/SB/08b are enclosed:
- Copies of all other items not listed above and listed in the attached forms PTO/SB/08a and PTO/SB/08b are not supplied because they were previously cited by or submitted to the Patent Office in a prior Application No. *, filed * and relied upon in this application for an earlier filing date under 35 U.S.C. § 120. See 37 C.F.R. § 1.98(d).

- Copies of those items which are marked with an asterisk (**) in the attached Form PTO-1499 were cited in a foreign examination report in a related case. A copy of the search report and the cited references not already of record in this application are attached hereto.

III. Concise Explanation of Relevance:

- A concise explanation of relevance of the items listed on forms PTO/SB/08a and PTO/SB/08b is not given.
- A concise explanation of relevance of [some of] the items listed on forms PTO/SB/08a and PTO/SB/08b is in the form of an English language copy of a Search Report from a foreign patent office, issued in a counterpart application, which refers to the relevant portions of the references (copy attached).

IV. Related Applications:

- Applicants bring to the Office's attention the following related, co-pending application(s):

V. Conclusion:

Citation of the above documents shall not be construed as:

1. an admission that the documents are necessarily prior art with respect to the instant invention;
2. a representation that a search has been made, other than as described above; or
3. an admission that the information cited herein is, or is considered to be, material to patentability as defined in § 1.56(b).

It is respectfully requested that the Examiner indicate consideration of the cited references by returning a copy of the attached forms PTO/SB/08a and PTO/SB/08b with initials or other appropriate marks. The Commissioner is hereby authorized to charge Deposit Account No. 50-2518, billing reference number: 7008282002 for any additional fees required in connection with the filing of this Information Disclosure Statement.

Respectfully submitted,

Dated: January 11, 2005

By: Antoinette F. Konski
Antoinette F. Konski
Registration No. 34,202

Bingham McCutchen LLP
Three Embarcadero Center, Suite 1800
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

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of

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Complete if Known

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned

Attorney Docket Number

NB 2006.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number Number – Kind Code ² (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
1	DE 32 29 169 A1		02-09-84	De Clercq et al.		
2	EP 0 311 107 A2		04-12-89	Stichting REGA VZW		
3	EP 0 311 108 A2		04-12-89	Stichting REGA VZW		
4	EP 0 316 592		05-24-89	Stichting REGA VZW		
5	GB 982 776		02-10-65	The Wellcome Foundation		
6	RO 88451		01-30-86	Antibiotics Enterprise, Iasi		X
7	WO 89/05817		06-29-89	Nucleic Acid Research Institute		
8	WO 90/03978		04-19-90	Stichting REGA VZW		
9	WO 91/17424		11-14-91	Vical, Inc.		
10	WO 92/19767		11-12-92	Terrapin Technologies, Inc.		
11	WO 93/06120		04-01-93	University of Rochester		

Examiner's Signature

Date Considered

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2.0 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

JAN 13 2005

PTO/SB/08A (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 2 of 5

Complete if Known

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS

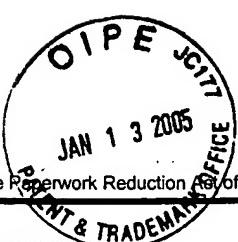
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
	12	WO 94/03467	02-17-94	Institute of Organic Chemistry & Biochemistry of the Academy of Sciences of the Czech Republic, et al.		
	13	WO 94/22483	10-13-94	Kozak, Alexander		
	14	WO 95/01806	01-19-95	Kondratyev, A.		
	15	WO 95/08556	03-30-95	Amersham International, Inc.		
	16	WO 95/12678	05-11-95	Connors, T. et al.		
	17	WO 96/03151	02-08-96	Springer et al.		
	18	WO 96/07413	04-04-96	University of Georgia Research Foundation & Yale University		

Examiner's Signature

Date Considered

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

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Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
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Attorney Docket Number	NB 2006.01

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		Number – Kind Code ² (if known)			

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		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
19	WO 96/10030		04-04-96	Isis Pharmaceuticals, Inc.		
20	WO 96/29336		09-26-96	Medical Research Council, University College Cardiff Consultants, Inc. Rega Foundation		
21	WO 96/33168		10-24-96	Kumiai Chemical Industry Co Ltd et al.		
22	WO 96/40088		12-19-96	Hostettler, Karl Y.		
23	WO 96/40708		12-19-96	La Jolla Pharmaceuticals, Inc.		
24	WO 96/40739		12-19-96	Terrapin Technologies, Inc.		
25	WO 97/25342		07-17-97	Terrapin Technologies, Inc.		

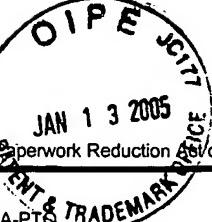
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet

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Complete if Known

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned

Attorney Docket Number

NB 2006.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS

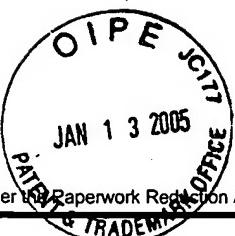
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
26	WO 97/28179		08-07-97	Fick, James & Israel, Mark		
27	WO 97/49717		12-31-97	Balzarini et al.		
28	WO 98/49177		11-05-98	University College Cardiff Consultants Limited		
29	WO 99/06072		02-11-99	Boehringer Mannheim Corp.		
30	WO 99/20741		04-29-99	Geron Corporation		
31	WO 99/23104		05-14-99	The Government of the United States of America represented by The Secretary of Health & Human Services		

Examiner's Signature

Date Considered

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 5 of 5

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Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned
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		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
32	WO 99/37753		07-29-99	NewBiotics, Inc.		
33	WO 00/18775		04-06-00	University College Cardiff Consultants Limited and Rega Foundation		
34	WO 00/33888		06-15-00	Dubois, V. et al.		
35	WO 01/07088		02-01-01	NewBiotics, Inc.		
36	WO 01/83501		11-08-01	University College Cardiff Consultants Limited and Rega Foundation		
37	WO 01/85749		11-15-01	University College Cardiff Consultants Limited and Rega Foundation		

Examiner's Signature		Date Considered	
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INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

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Sheet

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of

15

Complete if Known

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned

Attorney Docket Number

NB 2006.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
	1	ABRAHAM et al. "Synthesis and biological activity of aromatic amino acid phosphoramides of 5-fluoro-2'-deoxyuridine and 1-β-arabinofuranosylcytosine: Evidence of phosphoramidase activity" <i>J. Med. Chem.</i> (1996) 39 :4569-4575	
	2	AKDAS et al. "Glutathione S-transferase and multidrug-resistant phenotype in transitional cell carcinoma of the bladder" <i>Eur. Urol.</i> (1996) 29 (4):483-486	
	3	ALMASAN et al. "Genetic instability as a consequence of inappropriate entry into and progression through S-phase" <i>Cancer Metast. Rev.</i> (1995) 14 :59-73	
	4	ANDERSEN et al. "Detection of C-ERBB-2 related protein in sera from breast cancer patients" <i>Acta Oncol.</i> (1995) 34 (4):499-504	
	5	ANGLADA et al. "N,N'-cyclization of carbodiimides with 2-(bromomethyl)acrylic acid. A direct entry to the system 5-methylene-6H-pyrimidine-2,4-dione, A new class of thymine analogues" <i>J. Heterocyclic Chem.</i> (July-Aug. 1996) 33 :1259-1270	
	6	ANTELMAN et al. "Inhibition of tumor cell proliferation in vitro and in vivo by exogenous p110 ^{RB} , the retinoblastoma tumor suppressor protein" <i>Oncogene</i> (1995) 10 :697-704	
	7	ASAKURA and ROBINS, "Cerium(IV) catalyzed iodination at C5 of uracil nucleosides" <i>Tetrahedron Lett.</i> (1988) 29 (23):2855-2858	
	8	ASAKURA and ROBINS "Cerium(IV)-mediated halogenation at C-5 of uracil derivatives" <i>J. Org. Chem.</i> (1990) 55 :4928-4933	
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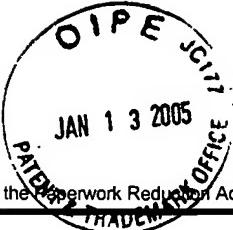
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Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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	14	BALZARINI et al. "Differential mechanism of cytostatic effect of (E)-5-(2-bromovinyl)-2'-deoxyuridine, 9-(1,3-dihydroxy-2-propoxymethyl)guanine, and other antiherpetic drugs on tumor cells transfected by the thymidine kinase gene of herpes simplex virus type 1 or type 2" <i>J. Biol. Chem.</i> (1993) 268 (9):6332-6337	
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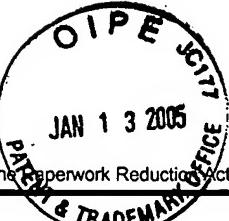
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	41	CHEN et al. "Sensitization of human breast cancer cells to cyclophosphamide and ifosfamide by transfer of a liver cytochrome P450 gene" <i>Cancer Res.</i> (Mar. 15, 1996) 56 :1331-1340	
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	71	FINER-MOORE et al. "Refined structures of substrate-bound and phosphate-bound thymidylate synthase from <i>Lactobacillus casei</i> " <i>J. Mol. Biol.</i> (1993) 232:1101-1116	
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet **7** of **15****Complete if Known**

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned

Attorney Docket Number **NB 2006.01****NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
	87	HANDFIELD and LEVESQUE "Strategies for isolation of in vitro expressed genes from bacteria" <i>FEMS Microbiol. Revs.</i> (1999) 23 :69-91	
	88	HAKIMELAHI et al. "Design, synthesis and structure-activity relationship of novel dinucleotide analogs as agents against herpes and human immunodeficiency viruses" "J. Med. Chem. (Nov. 10, 1995) 38(23) :4648-4659	
	89	HARDY et al. "Atomic structure of thymidylate synthase: Target for rational drug design" <i>Science</i> (Jan. 23, 1987) 235 :448-455	
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	92	HEIDELBERGER et al. "Fluorinated pyrimidines and their nucleosides" <i>Adv. Enzymol. Related Areas Mol. Biol.</i> (1983) 54 :57-119	
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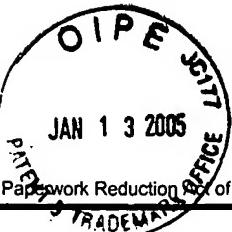
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Application Number	10/048,033
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First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned

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	100	HU et al. "Determination of absorption characteristics of AG337, a novel thymidylate synthase inhibitor, using a perfused rat intestinal model" <i>J. Pharmaceutical Sciences</i> (July 1998) 87(7):886-890	
	101	HUANG and SANTI "Active site general catalysts are not necessary for some proton transfer reactions of thymidylate synthase" <i>Biochemistry</i> (1997) 36:1869-1873	
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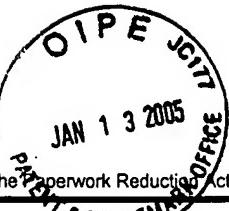
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Sheet

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Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned
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	115	KODAMA et al. "Evaluation of antiherpetic compounds using a gastric cancer cell line: Pronounced activity of BVDU against herpes simplex virus replication" <i>Microbiol. Immunol.</i> (1996) 40 (5):359-363	
	116	KUMAR et al. "Synthesis and biological evaluation of some cyclic phosphoramidate nucleoside derivatives" <i>J. Med. Chem.</i> (Sept. 1990) 33 (9):2368-2374	
	117	KUNDU et al. "Synthesis and biological activities of [E]-5-(2-acetylvinyl) uracils" <i>Eur. J. Med. Chem.</i> (1993) 28 :473-479	
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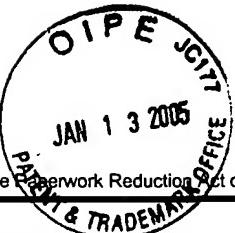
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Sheet

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First Named Inventor	H. Michael SHEPARD
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	130	MASTERS and ALTARDI "The nucleotide sequence of the cDNA coding for the human dihydrofolic acid reductase" <i>Gene</i> (1983) 21:59-63	
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Sheet

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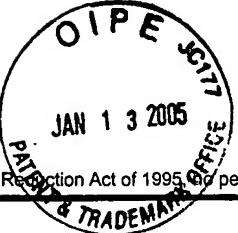
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	161	PETERS et al. "Thymidylate synthase and drug resistance" <i>Eur. J. Can.</i> (1995) 31A(7/8):1299-1305	
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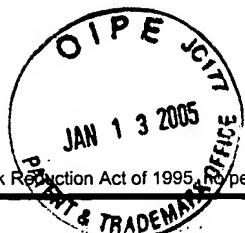
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of

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Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned

Attorney Docket Number

NB 2006.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
	176	SCHIFFER et al. "Crystal structure of human thymidylate synthase: A structural mechanism for guiding substrates into the active site" <i>Biochemistry</i> (1995) 34:16279-16287	
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				Application Number	10/048,033
				Filing Date	November 28, 2002
				First Named Inventor	H. Michael SHEPARD
				Art Unit	1615
				Examiner Name	Not Yet Assigned
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	192	SUKUMAR and BARBACID "Specific patterns of oncogene activation in transplacentally induced tumors" <i>PNAS USA</i> (Jan. 1990) 87:718-722	
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